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● *Original Contribution*

IN VIVO DOPPLER ULTRASOUND QUANTIFICATION OF TURBULENCE INTENSITY USING A HIGH-PASS FREQUENCY FILTER METHOD

MEGHAN L. THORNE,*† RICHARD N. RANKIN,‡ DAVID A. STEINMAN,¶ and DAVID W. HOLDSWORTH*†§

*Imaging Research Laboratories, Robarts Research Institute, London, ON; †Department of Medical Biophysics, University of Western Ontario, London, ON; ‡Department of Medical Imaging, University of Western Ontario, London, ON; §Department of Surgery, University of Western Ontario, London, ON; and ¶Biomedical Simulation Laboratory, University of Toronto, Toronto, ON, Canada

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Abstract—The objective of this investigation was to implement a high-pass frequency filter method to analyze Doppler ultrasound velocity waveforms and quantify turbulence intensity (TI) *in vivo*. Doppler velocity data were analyzed using two techniques, based on either ensemble averaging or high-pass frequency domain filtering of the periodic waveforms. The accuracy and precision of TI measurements were determined with controlled *in vitro* experiments, using a pulsatile-flow model of a stenosed carotid bifurcation. The high-pass filter technique was also applied *in vivo* to determine whether this technique could successfully distinguish between pertinent hemodynamic sites within the carotid artery bifurcation. Twenty-five seconds of Doppler audio data were acquired at three sites (common carotid artery [CCA], internal carotid artery [ICA] stenosis and distal ICA) within 10 human carotid arteries, and repeated three times. Doppler velocity data were analyzed using a ninth-order high-pass Butterworth filter with a 12-Hz inflection point. TI measured within the CCA and distal ICA was found to be significantly different ($p < 0.0001$) for moderate to nearly occluded carotid artery classifications. Also, TI measured within the distal ICA increased with stenosis severity, with the ability to distinguish between each stenosis class ($p < 0.05$). This investigation demonstrated the ability to precisely quantify TI using a conventional Doppler ultrasound machine in human subjects, without interfering with normal clinical protocols. (E-mail: david.holdsworth@imaging.robarts.ca)

Key Words: **High-pass frequency filter, Butterworth, MP3 recorder, Spectral analysis, Turbulence intensity, Coherent fluctuation, Incoherent fluctuation, Doppler ultrasound, Carotid artery disease, *in vivo*.**

INTRODUCTION

Carotid atherosclerosis is one of the leading causes of cardiovascular disease, accounting for 20–50% of all strokes and transient ischemic attacks (De Fabritiis et al. 2002; Fragata et al. 2006; Nandalur et al. 2006). All patients suspected of having atherosclerotic carotid artery disease will undergo a Doppler ultrasound examination (Gaitini and Soudack 2005), which is used to identify high-velocity jets within the internal carotid artery [ICA] that result from vessel stenosis (Sigel 1998). Doppler ultrasound (DUS) is the first-line imaging technique of choice because it is noninvasive, cost-effective and widely available (Osarumwense et al. 2005; Tahmasebpour et al. 2005; Titi et al. 2007). Although DUS has replaced angiography in many centers, often being the sole diagnostic tool before carotid endarterectomy (Hathout et al. 2005), current clinical diagnoses—based on peak systolic velocities (PSVs) alone—produce limited sensitivity (89%) and specificity (84%) for detection of stenoses suitable for surgery (Wardlaw et al. 2006). This inability to obtain precise information using an inherently quantitative technique such as DUS suggests fundamental limitations in the way Doppler spectra are interpreted and used. It has long been recognized that the current measurements of instantaneous PSV underuse and oversimplify the Doppler spectrum (Shung and Paeng 2003) and do not reflect our current knowledge of carotid atherosclerotic disease such as plaque characterization and hemodynamics within the vessel (Ricotta 2008). Investigations using other velocity-derived indices that take advantage of the full blood-velocity spectrum contained within the

Address correspondence to: D. W. Holdsworth, Imaging Research Laboratories, Robarts Research Institute, P.O. Box 5015, 100 Perth Drive, London, Ontario, N6A 5K8, Canada. E-mail: david.holdsworth@imaging.robarts.ca

Doppler signal, as opposed to a single instantaneous value, may provide more reliable hemodynamic information for increased diagnostic accuracy and reproducibility.

Recent advancements in Doppler spectral analysis—obtained over several cardiac cycles—have allowed us to move beyond observed Doppler peak systolic velocities provided by clinical equipment to calculate a variety of indices that may better describe the hemodynamics in the fluid system. Turbulence is one such hemodynamic phenomenon that is of particular interest, because it has been shown that disturbed flow and turbulence leads to endothelial cell dysfunction or injury of the vessel wall, which initiates platelet aggregation and clotting, predisposing the vessel to cardiovascular diseases such as atherosclerosis (Davies et al. 1986; Hademenos and Massoud 1997; Hutchison 1991). It has also been shown that disturbed flow and turbulence distal to vessel stenoses have been implicated as a risk for thromboembolic stroke (Sigel 1998) and as a potential indicator of significant stenoses (Ku 1997; May et al. 2001). Turbulence associated with a stenosis generates resistance that causes a sharp decrease in flow rate, leading to areas of recirculation in the flow field with higher values of vorticity, helicity and negative wall shear stress, which have been implicated as mechanisms for clotting (Banks and Bressloff 2007; Birchall et al. 2006) and significant thrombus production (Smith et al. 1972; Stein and Sabbah 1974). Turbulence near a plaque surface also results in pressure fluctuations that may cause plaque rupture (Loree et al. 1991). Disturbed flow is characterized by transient fluctuations in an otherwise laminar flow field, which causes the flow to deviate from streamlined motion. Yellin et al. (1966) explains that a region of disturbed flow may be described as turbulent, but true turbulence is self-preserving, rather than transient. The most popular method for quantifying apparent turbulence by DUS is turbulence intensity (TI), which directly measures incoherent fluctuating velocity components (Casty and Giddens 1984; Mann et al. 1987; Tarbell et al. 1986; Walburn et al. 1983). TI may provide the most robust characterization of turbulence (as opposed to quantification by spectral width, using either stenosis index or spectral-broadening index), potentially because of the confounding effects of machine-specific factors that result in inherent spectral broadening (Hoskins et al. 1999; Keeton et al. 1997). It is possible to quantify TI through ensemble averaging or through frequency filtering methods, where both of these analytical methods are used to decompose the Doppler signal into coherent pulsatile fluctuations and incoherent turbulent fluctuations.

The most common technique for characterizing turbulence from Doppler spectral data under pulsatile flow is through ensemble averaging. Past investigations have used this technique to quantify TI within diseased carotid arteries, demonstrating that it is feasible to quantify TI *in vivo* using a multichannel ultrasound unit (Casty and Giddens 1984). Ensemble averaging has also been implemented with clinical DUS equipment to quantify TI *in vitro* in the presence of pulsatile flow, including cycle-to-cycle cardiac variability (Thorne et al. 2009). Most recently, a clinical DUS machine was used to determine that TI measurements (calculated by ensemble averaging) could differentiate between ulcerated and non-ulcerated stenoses in carotid artery bifurcation models (Wong et al. 2009). The ensemble average method is ideal in any situation where an electrocardiogram (ECG)-gating signal is available, providing trigger information at the start of each cardiac cycle. Unfortunately, in a clinical environment the simultaneous acquisition of the patient's ECG signal is not typically part of the standard protocol for routine clinical carotid artery examinations and an alternative method is required to calculate Doppler parameters derived from periodic data. A previous investigation by Evans (1988) described a pulse-foot–seeking technique to approximate a gating signal from Doppler velocity data, which could be used instead of an ECG-gating pulse. Unfortunately, this technique is not feasible for noisy or turbulent pulsatile waveforms. An alternative to gated acquisition is Fourier frequency-domain analysis of Doppler mean velocities, where the implementation of a Fourier-domain high-pass frequency filter could be used to remove underlying coherent cyclic variations due to the cardiac cycle. A past study by Walburn et al. (1983) implemented both ensemble average and high-pass frequency filtering techniques on velocity information acquired by hot-film anemometry for the calculation of TI in the region of the aortic valve in patients. They found that high-pass frequency filtering of the velocity waveform may be more accurate than using the ensemble-average method in clinical implementation. The high-pass filtering technique was also used by Hjortdal et al. (1991) to quantify TI from velocities acquired by hot-film anemometry in the aortic valve of pigs, and by O'Toole et al. (1993) to quantify turbulence in patients with valvular aortic stenoses, based on pressure fluctuations. Another paper by Holdsworth et al. (1999) performed spectral analysis on 3560 cardiac cycles measured in the common carotid artery (CCA) and determined that the frequencies contributing to the coherent component of the carotid waveform are likely to occur between 0 and 12 Hz (Holdsworth 1999). The removal of this lower frequency band would result in a waveform comprised mainly of higher frequencies, including those produced by turbulent flow. The use of a high-pass frequency filter will potentially enable the acquisition and analysis of Doppler spectra *in vivo* without disruption of the current scan procedures.